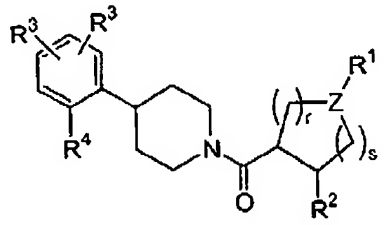
IN THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claim 1 (Currently Amended) A compound of structural formula I:



(I)

or a pharmaceutically acceptable salt thereof; wherein:

R^1 is selected from the group consisting of:

(1) hydrogen,
(2) amidino,
(3) C_{1-4} alkyliminoyl,
(4) C_{1-10} alkyl,
(5) $-(CH_2)_n-NR^7R^8$,
(6) $-(CH_2)_n-C_{3-7}$ cycloalkyl,
(7) $-(CH_2)_n$-phenyl,
(8) $-(CH_2)_n$-naphthyl, and
(9) $-(CH_2)_n$-heteroaryl,

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R^3, and wherein alkyl and cycloalkyl are unsubstituted or substituted with one to three groups independently selected from R^3 and oxo;

R^2 is selected from the group consisting of:

(1) phenyl,
(2) naphthyl, and
(3) heteroaryl,

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R^3;

each R^3 is independently selected from the group consisting of:

(1) hydrogen,
(2) C_{1-6} alkyl,

(3) -$(CH_2)_n$-phenyl,
(4) -$(CH_2)_n$-naphthyl,
(5) -$(CH_2)_n$-heteroaryl,
(6) -$(CH_2)_n$-heterocycloalkyl,
(7) -$(CH_2)_n$C3-7 cycloalkyl,
(8) halogen,
(9) OR^6,
(10) -$(CH_2)_nN(R^6)_2$,
(11) -$(CH_2)_nC{\equiv}N$,
(12) -$(CH_2)_nCO_2R^6$,
(13) NO_2,
(14) -$(CH_2)_nNR^6SO_2R^6$,
(15) -$(CH_2)_nSO_2N(R^6)_2$,
(16) -$(CH_2)_nS(O)_pR^6$,
(17) -$(CH_2)_nNR^6C(O)N(R^6)_2$,
(18) -$(CH_2)_nC(O)N(R^6)_2$,
(19) -$(CH_2)_nNR^6C(O)R^6$,
(20) -$(CH_2)_nNR^6CO_2R^6$,
(21) -$(CH_2)_nNR^6C(O)$-heteroaryl,
(22) -$(CH_2)_nC(O)NR^6N(R^6)_2$,
(23) -$(CH_2)_nC(O)NR^6NR^6C(O)R^6$,
(24) $O(CH_2)_nC(O)N(R^6)_2$,
(25) CF_3,
(26) CH_2CF_3,
(27) OCF_3, and
(28) OCH_2CF_3,

wherein phenyl, naphthyl, heteroaryl, cycloalkyl, and heterocycloalkyl are unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, oxo, C_{1-4} alkyl, trifluoromethyl, and C_{1-4} alkoxy, and wherein any methylene (CH_2) carbon atom in R^3 is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C_{1-4} alkyl, or wherein two substituents when on the same methylene (CH_2) group are taken together with the carbon atom to which they are attached to form a cyclopropyl group;

R^4 is selected from the group consisting of:

(1) -$(CH_2)_n$-$N(R^5)$-NR^5R^6,
(2) -$(CH_2)_n$-$N(R^5)$-$(CH_2)_q$-NR^5R^6,

(3) $-(CH_2)_n-N(R^5)-C(=NR^5)-NR^5R^6$,
(4) $-(CH_2)_n-N(R^5)-(CH_2)_q-N(R^5)-(C=NR^5)-NR^5R^6$,
(5) $-(CH_2)_n-N(R^5)-(CH_2)_n-C(R^5)(N(R^5)_2)-(CH_2)_q-OR^6$,
(6) $-(CH_2)_n-N(R^5)-(CH_2)_n-C(R^5)(N(R^5)_2)(CH_2)_n-R^6$,
(7) $-(CH_2)_n-N(R^5)-(CH_2)_n-C(R^5)(N(R^5)_2)(CH_2)_q-S(O)p-R^6$,
(8) $-(CH_2)_n-N(R^5)-(CH_2)_n-C(R^5)(N(R^5)_2)(CH_2)_q-NR^5R^6$,
(9) $-(CH_2)_n-N(R^5)-C(O)(CH_2)_n-C(R^5)(N(R^5)_2)(CH_2)_n-R^6$,
(10) $-(CH_2)_n-N(R^5)-C(O)(CH_2)_n-C(R^5)(N(R^5)_2)(CH_2)_q-S(O)p-R^6$,
(11) $-(CH_2)_n-N(R^5)-C(O)(CH_2)_n-C(R^5)(N(R^5)_2)(CH_2)_q-NR^5R^6$,
(12) $-(CH_2)_n-N(R^5)-C(O)(CH_2)_n-C(R^5)(N(R^5)_2)(CH_2)_q-O-R^6$, and
(13) $-(CH_2)_n-N(R^5)-R^9$,

wherein $(CH_2)_n$ is unsubstituted or substituted with one to three groups independently selected from halogen, C_{1-4} alkyl, hydroxy, oxo, and C_{1-4} alkoxy;

R^5 is selected from the group consisting of:

(1) hydrogen,
(2) C_{1-6} alkyl, and
(3) $C(O)C_{1-6}$ alkyl,

wherein alkyl is unsubstituted or substituted with one to three groups independently selected from halogen, C_{1-4} alkyl, hydroxy, oxo, and C_{1-4} alkoxy;

R^6 is selected from the group consisting of:

(1) hydrogen,
(2) C_{1-6} alkyl,
(3) $C(O)C_{1-6}$ alkyl,
(4) $-(CH_2)_nC_{3-7}$ cycloalkyl,
(5) $-(CH_2)_nC_{2-7}$ heterocycloalkyl,
(6) $-(CH_2)_n$-phenyl,
(7) $-(CH_2)_n$-naphthyl,
(8) $-(CH_2)_n$-heteroaryl, and
(9) $-(CH_2)_nC_{3-7}$ bicycloalkyl,

wherein alkyl, phenyl, heteroaryl, heterocycloalkyl, naphthyl, cycloalkyl, bicycloalkyl and $(CH_2)_n$ are unsubstituted or substituted with one to three groups indcpendently selected from halogen, C_{1-4} alkyl, hydroxy, and C_{1-4} alkoxy, or wherein two R^6 groups together with the atom to which they are attached form a 4- to 8-membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and $-NC_{1-4}$ alkyl;

each R^7 and R^8 is independently selected from the group consisting of:

(1) hydrogen,
(2) amidino,
(3) C_{1-4} alkyliminoyl,
(4) C_{1-10} alkyl,
(5) $-(CH_2)_n-C_{3-7}$ cycloalkyl,
(6) $-(CH_2)_n$-phenyl,
(7) $-(CH_2)_n$-naphthyl, and
(8) $-(CH_2)_n$-heteroaryl,

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R^3, and wherein alkyl and cycloalkyl are unsubstituted or substituted with one to three groups independently selected from R^3 and oxo;

R^9 is selected from the group consisting of:

(1) alanine,
(2) glycine,
(3) proline,
(4) cysteine,
(5) histidine,
(6) glutamine,
(7) aspartic acid,
(8) isoleucine,
(9) arginine,
(10) glutamic acid,
(11) lysine,
(12) serine,
(13) phenylalanine,
(14) leucine,
(15) threonine,
(16) tryptophan,
(17) methionine,
(18) valine,
(19) tyrosine,
(20) asparagine,
(21) 2-aminoadipic acid,
(22) beta-alanine,
(23) 2-aminoheptanedioic acid,

(24) 2-aminobutyric acid,
(25) 4-aminobutyric acid,
(26) 2,4-diaminobutyric acid,
(27) citrulline,
(28) cycloserine,
(29) norvaline,
(30) norleucine,
(31) ornithine,
(32) penicillamine,
(33) phenylglycine,
(34) phenylisoserine,
(35) phenylstatine,
(36) pipecolic acid,
(37) piperidine carboxylic acid,
(38) pyroglutamic acid,
(39) sarcosine,
(40) statine,
(41) allo-threonine,
(42) t-leucine,
(43) 2-aminoisobutyric acid, and
(44) 3-aminoisobutyric acid;

~~Z is selected from the group consisting of:~~

~~(1) $C(R^1)$, and~~

~~(2) N;~~

Z represents N;

r is 1 or 2;
s is 0, 1, or 2;
n is 0, 1, 2, or 3;
p is 0, 1, or 2; and
q is 1, 2, 3, or 4.

Claim 2 (Original) The compound of Claim 1 wherein R^1 is selected from the group consisting of: hydrogen, C_{1-6} alkyl, $-(CH_2)_{0-1}C_{3-6}$ cycloalkyl, and $-(CH_2)_{0-1}$-phenyl, wherein phenyl is unsubstituted or substituted with one to three groups independently selected from R^3, and alkyl and

cycloalkyl are optionally substituted with one to three groups independently selected from R^3 and oxo; and pharmaceutically acceptable salts thereof.

Claim 3 (Original) The compound of Claim 2 wherein R^2 is phenyl or thienyl, optionally substituted with one to three groups independently selected from R^3; and pharmaceutically acceptable salts thereof.

Claim 4 (Original) The compound of Claim 3 wherein R^2 is phenyl optionally substituted with one to three groups independently selected from R^3; and pharmaceutically acceptable salts thereof.

Claim 5 (Original) The compound of Claim 1 wherein each R^3 is independently selected from the group consisting of: C_{1-6} alkyl, $-(CH_2)_n$-phenyl, $-(CH_2)_n$-heteroaryl, $-(CH_2)_nC_{2-7}$ heterocycloalkyl, $-(CH_2)_nC_{3-7}$ cycloalkyl, halogen, OR^5, $-(CH_2)_nN(R^5)_2$, $-(CH_2)_nCO_2R^5$, NO_2, and CF_3, wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, C_{1-4} alkyl, trifluoromethyl, and C_{1-4} alkoxy, and wherein alkyl, cycloalkyl, heterocycloalkyl, and $(CH_2)_n$ are unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, oxo, C_{1-4} alkyl, trifluoromethyl, and C_{1-4} alkoxy, or wherein two substituents when on the same methylene (CH_2) group are taken together with the carbon atom to which they are attached to form a cyclopropyl group; and pharmaceutically acceptable salts thereof.

Claim 6 (Original) The compound of Claim 1 wherein R^4 is selected from the group consisting of:

(1) $-(CH_2)_n-N(R^5)-NH_2$,
(2) $-(CH_2)_n-N(R^5)-(CH_2)_q-NH_2$,
(3) $-(CH_2)_n-N(R^5)-(CH_2)_n-NR^5R^6$,
(4) $-(CH_2)_n-N(R^5)-(CH_2)_n-NHC_{1-6}$ alkyl,
(5) $-(CH_2)_n-N(R^5)-(CH_2)_n-N(C_{1-6}$ alkyl$)_2$,
(6) $-(CH_2)_n-N(R^5)-(CH_2)_n-NHC(O)C_{1-6}$ alkyl,
(7) $-(CH_2)_n-N(R^5)-(CH_2)_n-N(R^5)C(O)C_{1-6}$ alkyl,
(8) $-(CH_2)_n-N(R^5)-(CH_2)_n-N(C(O)C_{1-6}$ alkyl$)_2$,
(9) $-(CH_2)_n-N(R^5)-C(=NH)-NH_2$,
(10) $-(CH_2)_n-N(R^5)-(CH_2)_q-NH(C=NH)-NH_2$, $2n^52n2$
(11) $-(CH_2)_n-N(R^5)-(CH_2)_n-C(R^5)(NH_2)(CH_2)_q-OH$,
(12) $-(CH_2)_n-N(R^5)-(CH_2)_n-C(R^5)(NH_2)(CH_2)_q-OC_{1-6}$ alkyl,

(13) $-(CH_2)_n-N(R^5)-(CH_2)_n-C(R^5)(NH_2)(CH_2)_q-OR^6$,
(14) $-(CH_2)_n-N(R^5)-(CH_2)_n-C(R^5)(NH_2)(CH_2)_n$-heteroaryl,
(15) $-(CH_2)_n-N(R^5)-(CH_2)_n-C(R^5)(NH_2)(CH_2)_n-R^6$,
(16) $-(CH_2)_n-N(R^5)-(CH_2)_n-C(R^5)(NH_2)(CH_2)_q-SH$,
(17) $-(CH_2)_n-N(R^5)-(CH_2)_n-C(R^5)(NH_2)(CH_2)_q-S-C_{1-6}$ alkyl,
(18) $-(CH_2)_n-N(R^5)-(CH_2)_n-C(R^5)(NH_2)(CH_2)_q-S-R^6$,
(19) $-(CH_2)_n-N(R^5)-(CH_2)_n-C(R^5)(NH_2)(CH_2)_q-NH_2$,
(20) $-(CH_2)_n-N(R^5)-(CH_2)_n-C(R^5)(NH_2)(CH_2)_q-NHR^6$,
(21) $-(CH_2)_n-N(R^5)-(CH_2)_n-C(R^5)(NH_2)(CH_2)_q-NR^5R^6$,
(22) $-(CH_2)_n-N(R^5)-C(O)(CH_2)_n-C(R^5)(NH_2)(CH_2)_n$-heteroaryl,
(23) $-(CH_2)_n-N(R^5)-C(O)(CH_2)_n-C(R^5)(NH_2)(CH_2)_q-SH$,
(24) $-(CH_2)_n-N(R^5)-C(O)(CH_2)_n-C(R^5)(NH_2)(CH_2)_q-S-C_{1-6}$ alkyl,
(25) $-(CH_2)_n-N(R^5)-C(O)(CH_2)_n-C(R^5)(NH_2)(CH_2)_q-NR^5R^6$, and
(26) $-(CH_2)_n-N(R^5)-R^9$,

wherein alkyl and $(CH_2)_n$ are unsubstituted or substituted with one to three groups independently selected from halogen, C_{1-4} alkyl, hydroxy, oxo, and C_{1-4} alkoxy, and heteroaryl is unsubstituted or substituted with one to three groups independently selected from halogen, C_{1-4} alkyl, hydroxy, and C_{1-4} alkoxy; and pharmaceutically acceptable salts thereof.

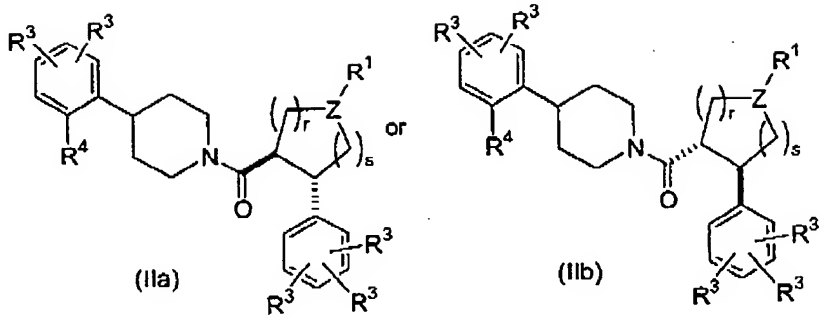
Claim 7 (Original) The compound of Claim 1 wherein R^6 is selected from the group consisting of: hydrogen, C_{1-6} alkyl, $C(O)C_{1-6}$ alkyl, and $-(CH_2)_n$-heteroaryl; and pharmaceutically acceptable salts thereof.

Claims 8-9 (Cancelled)

Claim 10 (Original) The compound of Claim 1 wherein r is 1 and s is 1; and pharmaceutically acceptable salts thereof.

Claim 11 (Original) The compound of Claim 1 wherein r is 2 and s is 1; and pharmaceutically acceptable salts thereof.

Claim 12 (Currently Amended) The compound of Claim 1 of structural formula IIa or IIb of the indicated *trans* relative stereochemical configuration:



or a pharmaceutically acceptable salt thereof; wherein:

R^1 is selected from the group consisting of: hydrogen, amidino, C_{1-4} alkyliminoyl, C_{1-6} alkyl, C_{5-6} cycloalkyl, $-(CH_2)_{0-1}$ phenyl, and $-(CH_2)_{0-1}$ heteroaryl, wherein phenyl and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R^3, and wherein alkyl and cycloalkyl are unsubstituted or substituted with one to three groups independently selected from R^3 and oxo;

each R^3 is independently selected from the group consisting of:

(1) hydrogen,
(2) C_{1-6} alkyl,
(3) $-(CH_2)_n$-phenyl,
(4) $-(CH_2)_n$-naphthyl,
(5) $-(CH_2)_n$-heteroaryl,
(6) $-(CH_2)_n$-heterocycloalkyl,
(7) $-(CH_2)_nC_{3-7}$ cycloalkyl,
(8) halogen,
(9) OR^{64},
(10) $-(CH_2)_nN(R^{64})_2$,
(11) $-(CH_2)_nC{\equiv}N$,
(12) $-(CH_2)_nCO_2R^{64}$,
(13) NO_2,
(14) $-(CH_2)_nNR^4SO_2R^{64}$,
(15) $-(CH_2)_nSO_2N(R^{64})_2$,
(16) $-(CH_2)_nS(O)_{0-1}R^{64}$,
(17) $-(CH_2)_nNR^{64}C(O)N(R^{64})_2$,
(18) $-(CH_2)_nC(O)N(R^{64})_2$,
(19) $-(CH_2)_nNR^{64}C(O)R^{64}$,

(20) $-(CH_2)_nNR^{64}CO_2R^{64}$,
(21) $-(CH_2)_nNR^{64}C(O)$-heteroaryl,
(22) $-(CH_2)_nC(O)NR^{64}N(R^{64})_2$,
(23) $-(CH_2)_nC(O)NR^{64}NR^{64}C(O)R^{64}$,
(24) $O(CH_2)_nC(O)N(R^{64})_2$,
(25) CF_3,
(26) CH_2CF_3,
(27) OCF_3, and
(28) OCH_2CF_3,

wherein phenyl, naphthyl, heteroaryl, cycloalkyl, and heterocycloalkyl are unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, oxo, C_{1-4} alkyl, trifluoromethyl, and C_{1-4} alkoxy, and wherein any methylene (CH_2) carbon atom in R^3 is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C_{1-4} alkyl, or wherein two substituents when on the same methylene (CH_2) group are taken together with the carbon atom to which they are attached to form a cyclopropyl group;

R^4 is selected from the group consisting of:

(1) $-(CH_2)$-$N(R^5)$-NR^5R^6,
(2) $-(CH_2)$-$N(R^5)$-$(CH_2)_{1-3}$-NR^5R^6,
(3) $-(CH_2)$-$N(R^5)$-$C(=NR^5)$-NR^5R^6,
(4) $-(CH_2)$-$N(R^5)$-$(CH_2)_{1-3}$-$N(R^5)$-$(C=NR^5)$-NR^5R^6,
(5) $-(CH_2)$-$N(R^5)$ -$(CH_2)_{0-2}$-$C(R^5)(N(R^5)_2)$-$(CH_2)_{1-2}$-OR^6,
(6) $-(CH_2)$-$N(R^5)$-$(CH_2)_{0-2}$-$C(R^5)(N(R^5)_2)(CH_2)_{1-2}$-$R^6$,
(7) $-(CH_2)$-$N(R^5)$-$(CH_2)_{0-2}$-$C(R^5)(N(R^5)_2)(CH_2)_{1-2}$-S-$R^6$,
(8) $-(CH_2)$-$N(R^5)$-$(CH_2)_{0-2}$-$C(R^5)(N(R^5)_2)(CH_2)_{1-4}$-$NR^5R^6$,
(9) $-(CH_2)$-$N(R^5)$-$C(O)(CH_2)_{0-2}$-$C(R^5)(N(R^5)_2)(CH_2)_{1-2}$-$R^6$,
(10) $-(CH_2)$-$N(R^5)$-$C(O)(CH_2)_{0-2}$-$C(R^5)(N(R^5)_2)(CH_2)_{1-2}$-S-$R^6$,
(11) $-(CH_2)$-$N(R^5)$-$C(O)(CH_2)_{0-2}$-$C(R^5)(N(R^5)_2)(CH_2)_{1-4}$-$NR^5R^6$, and
(12) $-(CH_2)$-$N(R^5)$-R^9,

wherein $(CH_2)_n$ is unsubstituted or substituted with one to three groups independently selected from halogen, C_{1-4} alkyl, hydroxy, oxo, and C_{1-4} alkoxy;

R^5 is selected from the group consisting of:

(1) hydrogen,
(2) C_{1-6} alkyl, and
(3) $C(O)C_{1-6}$ alkyl,

wherein alkyl is unsubstituted or substituted with one to three groups independently selected from halogen, C_{1-4} alkyl, hydroxy, oxo, and C_{1-4} alkoxy;

R^6 is selected from the group consisting of:

(1) hydrogen,
(2) C_{1-6} alkyl,
(3) $C(O)C_{1-6}$ alkyl,
(4) $-(CH_2)_nC_{3-7}$ cycloalkyl,
(5) $-(CH_2)_nC_{2-7}$ heterocycloalkyl,
(6) $-(CH_2)_n$-phenyl,
(7) $-(CH_2)_n$-naphthyl,
(8) $-(CH_2)_n$-heteroaryl, and
(9) $-(CH_2)_nC_{3-7}$ bicycloalkyl,

wherein alkyl, phenyl, heteroaryl, heterocycloalkyl, naphthyl, cycloalkyl, bicycloalkyl and $(CH_2)_n$ are unsubstituted or substituted with one to three groups independently selected from halogen, C_{1-4} alkyl, hydroxy, and C_{1-4} alkoxy, or wherein two R^6 groups together with the atom to which they are attached form a 4- to 8-membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and $-NC_{1-4}$ alkyl;

each R^7 and R^8 is independently selected from the group consisting of:

(1) hydrogen,
(2) amidino,
(3) C_{1-4} alkyliminoyl,
(4) C_{1-10} alkyl,
(5) $-(CH_2)_n-C_{3-7}$ cycloalkyl,
(6) $-(CH_2)_n$-phenyl,
(7) $-(CH_2)_n$-naphthyl, and
(8) $-(CH_2)_n$-heteroaryl,

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R^3, and wherein alkyl and cycloalkyl are unsubstituted or substituted with one to three groups independently selected from R^3 and oxo;

R^9 is selected from the group consisting of:

(1) alanine,
(2) glycine,
(3) proline,
(4) cysteine,
(5) histidine,

(6) glutamine,
(7) aspartic acid,
(8) isoleucine,
(9) arginine,
(10) glutamic acid,
(11) lysine,
(12) serine,
(13) phenylalanine,
(14) leucine,
(15) threonine,
(16) tryptophan,
(17) methionine,
(18) valine,
(19) tyrosine,
(20) asparagine,
(21) 2-aminoadipic acid,
(22) beta-alanine,
(23) 2-aminoheptanedioic acid,
(24) 2-aminobutyric acid,
(25) 4-aminobutyric acid,
(26) 2,4-diaminobutyric acid,
(27) citrulline,
(28) cycloserine,
(29) norvaline,
(30) norleucine,
(31) ornithine,
(32) penicillamine,
(33) phenylglycine,
(34) phenylisoserine,
(35) phenylstatine,
(36) pipecolic acid,
(37) piperidine carboxylic acid,
(38) pyroglutamic acid,
(39) sarcosine,
(40) statine,

(41) allo-threonine,

(42) t-leucine,

(43) 2-aminoisobutyric acid, and

(44) 3-aminoisobutyric acid;

~~Z is selected from the group consisting of:~~

~~(1)C(R^1), and~~

~~(2) N;~~

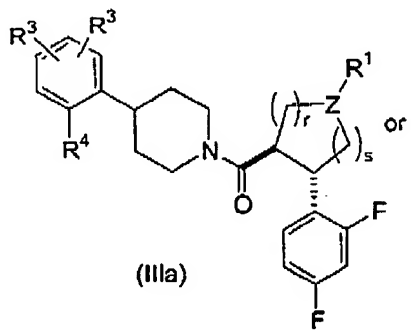
Z represents N;

r is 1 or 2;

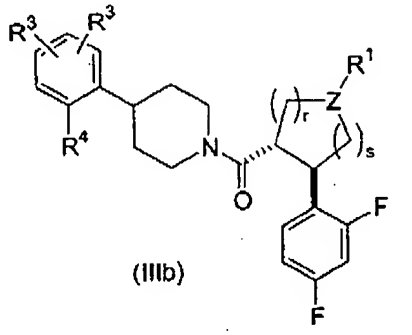
s is 0, 1, or 2; and

n is 0, 1, 2, 3 or 4.

Claim 13(Currently Amended) The compound of Claim 1 of structural formula IIIa or IIIb of the indicated *trans* relative stereochemical configuration:



(IIIa) or



(IIIb)

or a pharmaceutically acceptable salt thereof; wherein:
R^1 is selected from the group consisting of: hydrogen, C_{1-4} alkyl, and -$(CH_2)_{0-1}$ phenyl;

each R^3 is independently selected from the group consisting of:

(1) hydrogen,

(2) C_{1-6} alkyl,

(3) -$(CH_2)_n$-phenyl,

(4) -$(CH_2)_n$-naphthyl,

(5) -$(CH_2)_n$-heteroaryl,

(6) -$(CH_2)_n$-heterocycloalkyl,

(7) -$(CH_2)_n C_{3-7}$ cycloalkyl,

(8) halogen,

(9) OR^{64},
(10) $-(CH_2)_nN(R^{64})_2$,
(11) $-(CH_2)_nC{\equiv}N$,
(12) $-(CH_2)_nCO_2R^{64}$,
(13) NO_2,
(14) $-(CH_2)_nNR^{64}SO_2R^{64}$,
(15) $-(CH_2)_nSO_2N(R^{64})_2$,
(16) $-(CH_2)_nS(O)_{0-1}R^{64}$,
(17) $-(CH_2)_nNR^{64}C(O)N(R^{64})_2$,
(18) $-(CH_2)_nC(O)N(R^{64})_2$,
(19) $-(CH_2)_nNR^{64}C(O)R^{64}$,
(20) $-(CH_2)_nNR^{64}CO_2R^{64}$,
(21) $-(CH_2)_nNR^{64}C(O)$-heteroaryl,
(22) $-(CH_2)_nC(O)NR^{64}N(R^{64})_2$,
(23) $-(CH_2)_nC(O)NR^{64}NR^{64}C(O)R^{64}$,
(24) $O(CH_2)_nC(O)N(R^{64})_2$,
(25) CF_3,
(26) CH_2CF_3,
(27) OCF_3, and
(28) OCH_2CF_3,

wherein phenyl, naphthyl, heteroaryl, cycloalkyl, and heterocycloalkyl are unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, oxo, C_{1-4} alkyl, trifluoromethyl, and C_{1-4} alkoxy, and wherein any methylene (CH_2) carbon atom in R^3 is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and C_{1-4} alkyl, or wherein two substituents when on the same methylene (CH_2) group are taken together with the carbon atom to which they are attached to form a cyclopropyl group;

R^4 is selected from the group consisting of:

(1) $-(CH_2)$-$N(R^5)$-NR^5R^6,
(2) $-(CH_2)$-$N(R^5)$-$(CH_2)_{1-3}$-NR^5R^6,
(3) $-(CH_2)$-$N(R^5)$-$C(=NR^5)$-NR^5R^6,
(4) $-(CH_2)$-$N(R^5)$-$(CH_2)_{1-3}$-$N(R^5)$-$(C=NR^5)$-NR^5R^6,
(5) $-(CH_2)$-$N(R^5)$-$(CH_2)_{0-2}$-$C(R^5)(N(R^5)_2)$-$(CH_2)_{1-2}$-OR^6,
(6) $-(CH_2)$-$N(R^5)$-$(CH_2)_{0-2}$-$C(R^5)(N(R^5)_2)(CH_2)_{1-2}$-$R^6$,
(7) $-(CH_2)$-$N(R^5)$-$(CH_2)_{0-2}$-$C(R^5)(N(R^5)_2)(CH_2)_{1-2}$-S-$R^6$,
(8) $-(CH_2)$-$N(R^5)$-$(CH_2)_{0-2}$-$C(R^5)(N(R^5)_2)(CH_2)_{1-4}$-$NR^5R^6$,

(9) -(CH_2)-$N(R^5)$-$C(O)(CH_2)_{0-2}$-$C(R^5)(N(R^5)_2)(CH_2)_{1-2}$-$R^6$,
(10) -(CH_2)-$N(R^5)$-$C(O)(CH_2)_{0-2}$-$C(R^5)(N(R^5)_2)(CH_2)_{1-2}$-S-$R^6$,
(11) -(CH_2)-$N(R^5)$-$C(O)(CH_2)_{0-2}$-$C(R^5)(N(R^5)_2)(CH_2)_{1-4}$-$NR^5R^6$, and
(12) -(CH_2)-$N(R^5)$- R^9,

wherein $(CH_2)_n$ is unsubstituted or substituted with one to three groups independently selected from halogen, C_{1-4} alkyl, hydroxy, oxo, and C_{1-4} alkoxy;

R^5 is selected from the group consisting of:

(1) hydrogen,
(2) C_{1-6} alkyl, and
(3) $C(O)C_{1-6}$ alkyl,

wherein alkyl is unsubstituted or substituted with one to three groups independently selected from halogen, C_{1-4} alkyl, hydroxy, oxo, and C_{1-4} alkoxy;

R^6 is selected from the group consisting of:

(1) hydrogen,
(2) C_{1-6} alkyl,
(3) $C(O)C_{1-6}$ alkyl,
(4) -$(CH_2)_nC_{3-7}$ cycloalkyl,
(5) -$(CH_2)_nC_{2-7}$ heterocycloalkyl,
(6) -$(CH_2)_n$-phenyl,
(7) -$(CH_2)_n$-naphthyl,
(8) -$(CH_2)_n$-heteroaryl, and
(9) -$(CH_2)_nC_{3-7}$ bicycloalkyl,

wherein alkyl, phenyl, heteroaryl, heterocycloalkyl, naphthyl, cycloalkyl, bicycloalkyl and $(CH_2)_n$ are unsubstituted or substituted with one to three groups independently selected from halogen, C_{1-4} alkyl, hydroxy, and C_{1-4} alkoxy, or wherein two R^6 groups together with the atom to which they are attached form a 4- to 8-membered mono- or bicyclic ring system optionally containing an additional heteroatom selected from O, S, and -NC_{1-4} alkyl;

each R^7 and R^8 is independently selected from the group consisting of:

(1) hydrogen,
(2) amidino,
(3) C_{1-4} alkyliminoyl,
(4) C_{1-10} alkyl,
(5) -$(CH_2)_n$-C_{3-7} cycloalkyl,
(6) -$(CH_2)_n$-phenyl,
(7) -$(CH_2)_n$-naphthyl, and

(8) -$(CH_2)_n$-heteroaryl,

wherein phenyl, naphthyl, and heteroaryl are unsubstituted or substituted with one to three groups independently selected from R^3, and wherein alkyl and cycloalkyl are unsubstituted or substituted with one to three groups independently selected from R^3 and oxo;

R^9 is selected from the group consisting of:

(1) alanine,
(2) glycine,
(3) proline,
(4) cysteine,
(5) histidine,
(6) glutamine,
(7) aspartic acid,
(8) isoleucine,
(9) arginine,
(10) glutamic acid,
(11) lysine,
(12) serine,
(13) phenylalanine,
(14) leucine,
(15) threonine,
(16) tryptophan,
(17) methionine,
(18) valine,
(19) tyrosine,
(20) asparagine,
(21) 2-aminoadipic acid,
(22) beta-alanine,
(23) 2-aminoheptanedioic acid,
(24) 2-aminobutyric acid,
(25) 4-aminobutyric acid,
(26) 2,4-diaminobutyric acid,
(27) citrulline,
(28) cycloserine,
(29) norvaline,
(30) norleucine,

(31) ornithine,
(32) penicillamine,
(33) phenylglycine,
(34) phenylisoserine,
(35) phenylstatine,
(36) pipecolic acid,
(37) piperidine carboxylic acid,
(38) pyroglutamic acid,
(39) sarcosine,
(40) statine,
(41) allo-threonine,
(42) t-leucine,
(43) 2-aminoisobutyric acid, and
(44) 3-aminoisobutyric acid;

~~Z is selected from the group consisting of:~~

~~(1) C(R^1), and~~

~~(2) N;~~

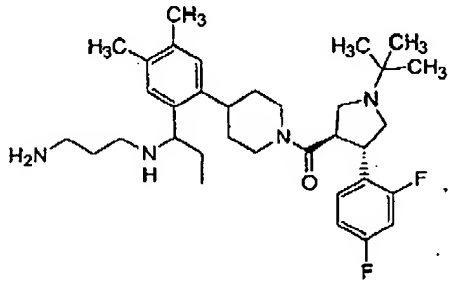
Z represents N;

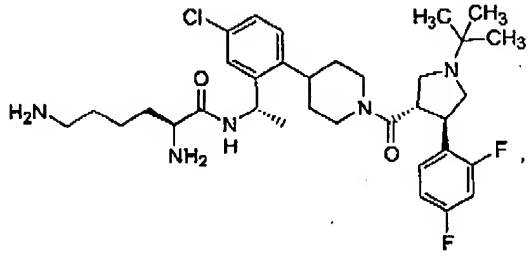
r is 1 or 2;

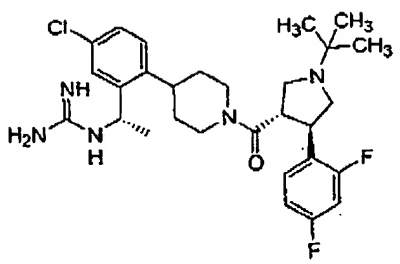
s is 0, 1, or 2; and

n is 0, 1, 2, 3, or 4.

Claim 14 (Original) The compound of Claim 13 selected from the group consisting of:



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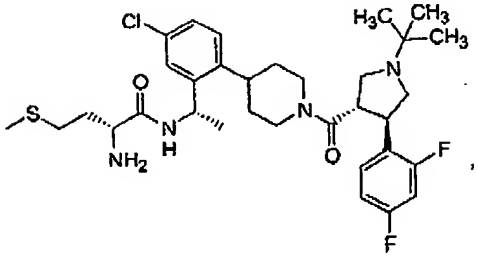
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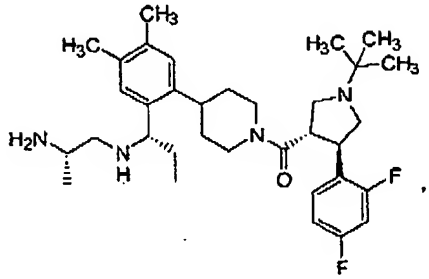
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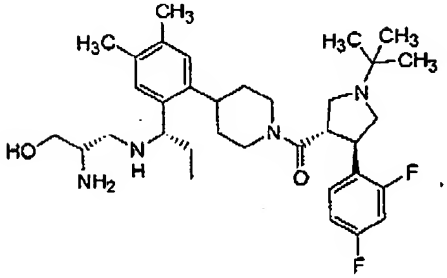
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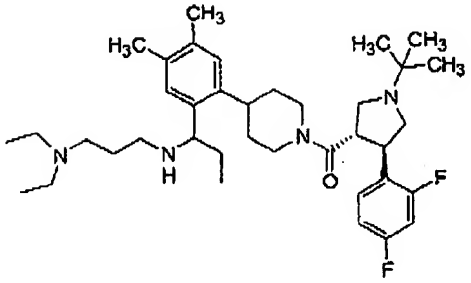
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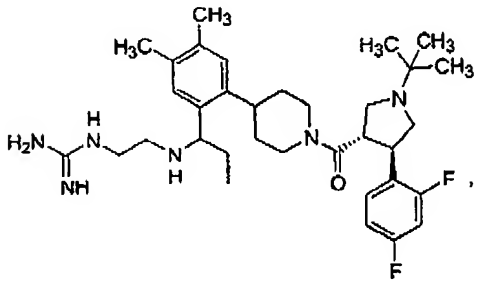
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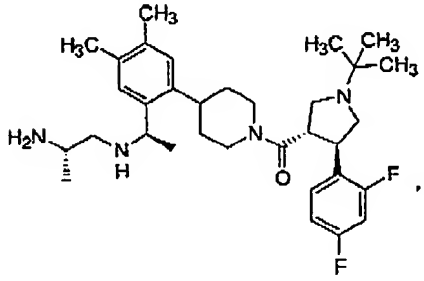
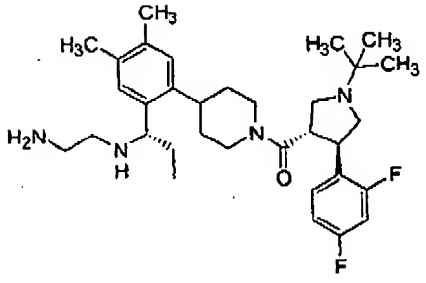
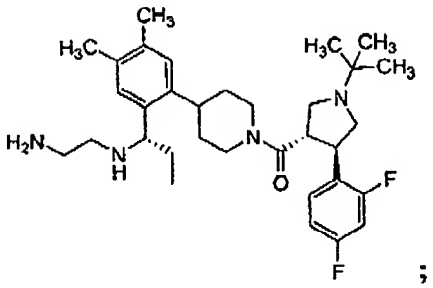

, and


;

or a pharmaceutically acceptable salt thereof.

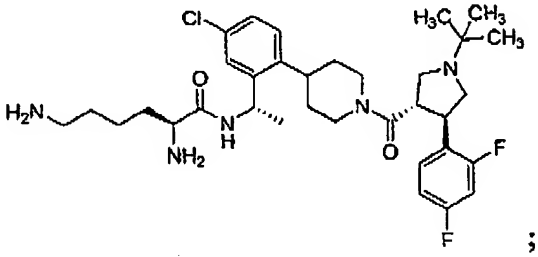
Claim 15(Original) The compound of Claim 14 which is:



;

or a pharmaceutically acceptable salt thereof.

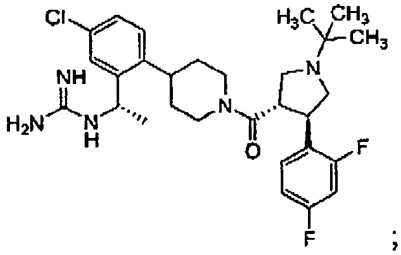
Claim 16 (Original) The compound of Claim 14 which is:



;

or a pharmaceutically acceptable salt thereof.

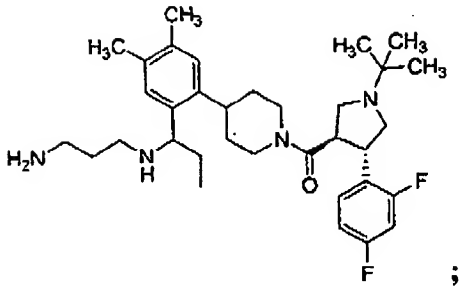
Claim 17 (Original) The compound of Claim 14 which is:



;

or a pharmaceutically acceptable salt thereof.

Claim 18 (Original) The compound of Claim 14 which is:



;

or a pharmaceutically acceptable salt thereof.

Claim 19 (Cancelled)

Claim 20 (Currently amended) A method for the treatment or prevention of obesity, or diabetes mellitus, ~~male sexual dysfunction, female sexual dysfunction or erectile dysfunction~~ in a mammal in need thereof which comprises administering to the mammal a therapeutically or prophylactically effective amount of a compound according to Claim 1.

Claims 21-23 (Cancelled)

Claim 24 (Original) A pharmaceutical composition which comprises a compound of Claim 1 and a pharmaceutically acceptable carrier.

Claims 25-30 (Cancelled)

Claim 31 (Currently Amended) A method of treating ~~or preventing~~ diabetes or obesity in a mammal in need thereof comprising administering to the mammal a therapeutically effective ~~or prophylactically effective~~ amount of a compound of Claim 1 in combination with an insulin sensitizer, an insulin mimetic, a sulfonylurea, an α-glucosidase inhibitor, a HMG-CoA reductase inhibitor, a serotonergic agent, a β3-adrenoreceptor agonist, a neuropeptide Y1 antagonist, a neuropeptide Y5 antagonist, a pancreatic lipase inhibitor, a cannabinoid CB_1 receptor antagonist or inverse agonist, a melanin-concentrating hormone receptor antagonist, a bombesin receptor subtype 3 agonist, a ghrelin receptor antagonist, or a dipeptidyl peptidase IV inhibitor.

Claim 32 (Previously Presented) A method of treating or preventing an obesity-related disorder selected from the group consisting of: overeating, binge eating, and bulimia, hypertension, diabetes, elevated plasma insulin concentrations, insulin resistance, dyslipidemias, hyperlipidemia, endometrial,

breast, prostate and colon cancer, osteoarthritis, obstructive sleep apnea, cholelithiasis, gallstones, heart disease, abnormal heart rhythms and arrythmias, myocardial infarction, congestive heart failure, coronary heart disease, sudden death, stroke, polycystic ovary disease, craniopharyngioma, the Prader-Willi Syndrome, Frohlich's syndrome, GH-deficient subjects, normal variant short stature, Turner's syndrome, metabolic syndrome, insulin resistance syndrome, sexual and reproductive dysfunction, infertility, hypogonadism, hirsutism, obesity-related gastro-esophageal reflux, Pickwickian syndrome, cardiovascular disorders, inflammation, systemic inflammation of the vasculature, arteriosclerosis, hypercholesterolemia, hyperuricaemia, lower back pain, gallbladder disease, gout, and kidney cancer, cardiac hypertrophy and left ventricular hypertrophy, in a mammal in need thereof which comprises administering to the mammal a therapeutically or prophylactically effective amount of a compound according to Claim 1.

Claims 33-42 (Cancelled)